March 26, 1976

MEMORANDUM

TO: W. T. Hoyt

CC: AY
WUG
RCH
WK

FROM: Leonard S. Zahn

SUBJECT: American Academy of Allergy, San Juan, P.R., March 6-10, 1976

One normally would not expect controversy at a meeting of this kind, but a slight flap did arise following presentation of a paper on a CTR-sponsored project that appeared somewhat to take tobacco off the hook in the area of "passive smoking."

The paper, titled "Tobacco Allergy: Fact or Fancy?", was by John C. McDougall and Gerald Gleich of Rochester's Mayo Clinic and was read by the former. In substance, it said they were unable to find allergy to tobacco and tobacco smoke in the subjects they studied.

Following the presentation, Bernard Sussman of Memphis read a prepared statement in which he said the report did not mention whether the study subjects were allergic, and presumably they were not. In a study he did, all the subjects, though nonsmokers, were clinically sensitive to tobacco smoke. Sussman continued:

It has been known for several years that the RAST (radioallergosorbent test) for tobacco was negative even in the most sensitive patients. Children exposed early in life to tobacco smoke show sensitivity by age 5; avoidance of tobacco smoke is impossible when one or both parents smoke. The incidence of tobacco sensitivity is about 16% of the allergic population -- about 8-million people. "We feel that this has become a problem of profound importance and the major challenge to all allergists -- failure to recognize this problem and to take an active role in its management and treatment -- would be a disservice to millions of patients who look to us for proper advice and treatment."

A Canadian physician (I was unable to identify him) commented on the fact that the Mayo people did find some kind of tobacco allergen and they might find others, if they continued their research. McDougall responded that the skin test results were likely nonspecific. Commercially available cigarettes were used, he said, and they were found to contain ragweed pollen and mold spores; these may have been responsible for the allergic responses, not the

Leonard Zahn and Associates, Inc. PUBLIC RELATIONS COUNSEL
P. O. BOX 523 • 13 LINCOLN ROAD • GREAT NECK, N.Y. 11021 • (212) 895-7445

tobacco itself.

Then Joseph Harkavy of New York, an elderly, well-known allergist, made a rambling, emotional statement in which he said the Mayo work was a "useless observation." He has been interested in tobacco for 40 years, he said, and has found that patients sensitive to pollen will give a positive reaction to tobacco. He said he has immunized rabbits with tobacco protein and the animals developed coronary artery disease. They also got gangrene of the toes, he said. (The session chairman cut Harkavy short.)

Correct - Library file is complete - WK

As McDougall and Gleich left the meeting hall, Harkavy accosted them in the foyer and accused them of a "criminal act" with their report. The tobacco industry, he said, would use the research to help sell more cigarettes and thereby kill more people. Harkavy was shouting so loudly that a room monitor had to admonish him.

Harkavy later went to the press room where he sought to persuade the few writers covering the meeting to ignore the McDougall-Gleich report. He accused the press of helping the industry sell more cigarettes! Voluble and red-faced, Harkavy demanded of the academy's press relations head how the report got on the program, who titled it, etc. He said he would do his utmost to prevent its publication in the academy's journal. (A freelance writer-columnist, Fraser Kent of Miami, winked at me, turned to Harkavy and said, "Doctor, that's such a terrific report that I'm going to put it on the front page." Harkavy exploded anew.)

A summary of the McDougall-Gleich report:

Three extracts were made from commercially available cigarettes: an aqueous extract made by homogenizing tobacco in phosphate buffered saline, an aqueous extract prepared by bubbling mainstream smoke through distilled water, and an extract made by bubbling smoke through human serum albumin (HSA). In tests with rabbits and guinea pigs, antibody was found to tobacco extract in the sera of animals injected with tobacco extract but no antibody was found to tobacco smoke or smoked HSA.

Serum was collected from 174 human subjects classified as to smoking history and bronchial secretions were collected from 12 smokers and nonsmokers. Serum also was collected from 10 persons who considered themselves allergic to tobacco or tobacco smoke (eye irritation, cough, nasal congestion etc.); these 10 were selected from 30 persons who answered a newspaper ad asking for advertisements. No antibody activity was found to any of the three possible antigens in any human serum or bronchial secretions.

Checking the possibility of IgE response to tobacco or tobacco smoke, the sera of the subjects was tested with smoked HSA in a RAST system. Activity was low and there was no significant difference among the three groups tested.

A protein from tobacco was partically purified (which was antigenic in rabbits) and was used for skin tests in normal subjects and in persons who considered themselves allergic to tobacco or its smoke. There were 7 positive and 8 negative reactors. The positives all had elevated total serum IgE and the negatives had a normal total serum. No person with a positive skin test reaction to tobacco had a normal IgE. The presence of symptoms on exposure to tobacco or its smoke did not correlate with a positive skin test to tobacco protein.

The two scientists concluded: "We can say there is a protein in tobacco which is antigenic in rabbits. We were unable to detect any humoral immune response to this protein or to tobacco smoke or smoke-treated human serum albumin in the serum and bronchial secretions of human subjects. We did find that some subjects have positive skin test responses to tobacco protein, but that this does not correlate with the presence or absence of these symptoms. We were also unable to demonstrate any specific IgE binding to tobacco protein or smoke-treated human serum albumin in the serum of patients who reported allergic symptoms to tobacco or tobacco smoke.

"It is possible that we have not screened the proper population in looking for allergy to tobacco or tobacco smoke. It would be of interest to perform skin tests and RAST studies on subjects who are exposed occupationally to tobacco dust. Another avenue of investigation that might prove fruitful is that of cellular immunity to the tobacco or tobacco smoke. It should perhaps be stressed that a negative study such as this one does not imply that persons with other allergies should expose themselves to tobacco smoke without fear of provoking symptoms but it is likely that those symptoms they experience are due to nonspecific irritation."

-0-

Gareth Green of Burlington, Vt., opened the post-graduate course of the meeting with a rather basic lecture on "Factors Affecting Lung Clearance Mechanisms." His talk was so basic, at least at the beginning, that a number of doctors soon left the hall. More than half-way through his lecture, Green turned to tobacco and described much of what he has already published. Other data seemed to be new.

He is using fiberoptic bronchoscopy to lavage cells (alveolar macrophages) from the lungs of humans. Preliminary results indicate that about 2-3 times the number of cells can be obtained from smokers than from nonsmokers. It's not known whether this represents a successful response to a challenge or a hazard. Possibly it's a combination of both.

He's testing macrophages with the (Cambridge filtered) gas phase of cigarette smoke. There seems to be a rise in particle uptake and intracellular activity when cells are exposed to increasing amounts of gas phase smoke.

In testing cells from smokers and nonsmokers, he has found that cells from the former show much more variability than do those from the latter in response to subsequent exposure to smoke. This indicates, he said, that there is no adaptation in some situations while in other situations there may be some adaptation.

Cigarette smoke is a "fantastically rich material in terms of chemical agents," Green said. By fractionating the gas phase (gas chromatography), one can identify many areas not toxic to alveolar macrophages and others that are quite toxic. The major toxic material in the gas phase is acrolein and this agent is present in an amount 1500 times that set for industrial exposure.

The gas phase adversely affects the energy metabolizing systems of the lung, suppressing certain pathways and thereby causing damage and disease.

Some laboratory evidence exists to show a protective effect by the chemical cysteine in regard to particle uptake and intracellular activity, Green said. It is "perhaps a sign of things to come" that one can influence the activity of the macrophages by chemical means.

-0-

With the exception of the McDougall and Green presentations, there was little mention of tobacco in the nearly 200 papers delivered at the meeting. Many reports dealt with diagnosis and treatment of allergic diseases; a number were concerned with efforts and/or theories involving specific mechanisms, and some reported advances.

Press coverage was extremely limited: a writer for the news section of the Journal of the AMA, the aforementioned Fraser Kent (who writes a column for a group of weekly papers, two freelancers from Ireland, and a reporter from a medical publishing company in Rockville, Md. Dicussions were held with them about the McDougall report and a follow-up with certain media was made on my return.

But at Cincinnati's Shriners Burns Institute, chief of staff Bruce MacMillan reports that 30% of the patients have been getting fungal infections since "intensive" *Sulfamylon* therapy was introduced three or four years ago. He adds that only 2% of the infections become invasive, and that 90% of these are fatal.

Says Dr. Boswick, "Doctors have known about the possibility of increased fungal infection for years. It doesn't surprise anybody." Dr. MacMillan agrees, and adds that other antibacterial agents—silver nitrate and "especially" gentamicin—have the same effect.

All three doctors defend *Sulfamylon*, holding that its advantages far outweigh the risk of mycotic infection and that it is still very much needed. Dr. MacMillan calls it the "best and most effective antibacterial drug for burn patients" and adds that since his institute began using the anti-yeast agent, nystatin, along with *Sulfamylon*, the rate of fungal infection has leveled off. Dr. Goodwin says that before *Sulfamylon* arrived, bacterial sepsis was the leading killer of burn patients. "Now it's way down the list of the culprits involved."

A Winthrop spokesman said Dr. Goodwin's data "corroborate the well-known fact that saprophytic fungal organisms may be the causes of superinfection if bacteria are eliminated. It is not too surprising that mycotic infections of major burn wounds have occurred following topical antibacterial therapy." He noted that the *Sulfamylon* cream labeling warns: "Fungal colonization in and below the eschar may occur concomitantly with reduction of bacterial growth in the burn wound. However, fungal dissemination through the infected burn wound is rare."

"nothing but chance—not even rough play."

Rough play is the rule in hockey, especially when the Stanley Cup is at stake. Pat Stapleton of the Chicago Black Hawks got his face badly gashed early in the series against Montreal, but was back in action with 52 stitches in time to bolster his team's defense in the remaining games.

The Canadiens were generally fit, although playing without defenseman Serge Savard, who re-broke his leg in a game last year. Savard had open reduction with internal fixation when he took a low check that caused the bone to fracture through the screw holes. Does that finish his career? According to Dr. Edward C. Percy of Montreal General Hospital, "Serge hopes to be back in play by next season."

LOOSENING TIES

BLUE CROSS, AHA DISENGAGE

Blue Cross and the American Hospital Association have agreed "in principle" that each will stop naming members to the other's governing board, and that instead, they will enlarge their joint committee and have it meet more often. Currently, two of the 26 Blue Cross governors are AHA members, and three of the 25 AHA trustees are Blue Cross representatives.

Both associations say the agreement remains highly tentative and that it is subject to evaluation by study groups. In fact, by the time the Blue Cross board reconvenes in July and the AHA board the following month, the entire situation could very well be reversed.

Officials of the associations acknowledge that congressional storms of their close ties helped prod them into the agreement. "Blue Cross plans pay hospitals a lot of money," says AHA Executive Vice President Edwin Crosby, "and many people now feel that any negotiations between the groups must be conducted at arm's length."

The two groups are also considering making the Blue Cross symbol Blue Cross property. It now belongs to AHA, and any group wanting to use it must satisfy the standards of the AHA.

For The Record

Women's coats made with cloth containing asbestos may cause lung cancer in the garment workers who made them and even in the women who wear them, warns Dr. Irving J. Selikoff, head of environmental medicine at New York's Mount Sinai Medical Center. He says rubbing a coat made with asbestos produces asbestos levels in the air 10,000 times normal, and that once inhaled, the particles are neither dissolved nor expelled. "The host may suffer no ill effects for years, but the danger of lung cancer or some other asbestos-induced malady remains."

*

Legal restrictions on prescribing contraceptives for minors should be abolished, and decisions on abortions should be left to doctors and their patients, says the American College of Obstetricians and Gynecologists. A survey last year indicated that most obstetricians and gynecologists would provide contraception for minors without parental consent (MWN, Feb. 26).

*

The agent in cigarette smoke that damages pulmonary alveolar macrophages is acrolein, reports University of Vermont researcher Dr. Gareth Green. In in vitro tests, he found that the chemical's toxicity is caused by its action on the enzyme glyceraldehyde-3-phosphate dehydrogenase, with resultant suppression of glycolosis and of the energy production needed for phagocytosis. Acrolein, an industrial chemical, occurs in cigarette smoke at levels 1,500 times higher than recognized limits for industrial exposure.

*

Wearers of nuclear-powered pacemakers can cross Western European borders, now that a special agreement has been drawn up by Austria, Denmark, France, West Germany, Spain, Sweden, and Switzerland. The agreement eases restrictions on international movement of radioactive materials but still requires pacemakers to conform to safety guidelines.